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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,710	08/05/2003	Richard J. Yarwood	03762.012500.3	1897
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Fitzpatrick Cella (Catalent) 30 Rockefeller Plaza New York, NY 10112			EXAMINER SOROUSH, ALI	
			ART UNIT 1616	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/635,710	Applicant(s) YARWOOD ET AL.	
	Examiner ALI SOROUGH	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 January 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/02/2009 has been entered.

Status of the Claims

Claims 24 and 25 are currently amended and claims 1-23 and 39 are cancelled. Therefore, claims 24-38 are currently pending examination for patentability.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Double Patenting

1. The rejection of claims 24-38 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, and 4-16 of U.S. Patent No. 6,726, 928 B2 **is maintained**. Applicant's argument that once all other issues concerning the pending application have been addressed they will then file a terminal disclaimer is acknowledged. The rejection is therefore maintained until the terminal disclaimer is filed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. The rejection of claims 24, 26-30, 32-34, and 36 under 35 U.S.C. 103(a) as being unpatentable over Gregory et al. (US 4305502, Published 12/15/1981) in view of Ince et al. (US 4657929, Published 04/14/1987) **is maintained.**

Applicant Claims

Applicant claims a process for the preparation of a solid, rapidly disintegrating dosage form comprising a pharmaceutically active substance in an aqueous or alcohol solvent and further comprising a carrier materials (i.e. gelatin), rendering the active substance less soluble. The process further comprises the composition being filled into a plurality of mold pockets in a film and frozen, which is further freeze-dried, or vacuum dried to remove the solvent.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Gregory et al. teaches, "The invention relates to packages containing shaped articles carrying chemicals, particularly to pharmaceutical dosage forms carrying pharmaceuticals. The shaped articles, which disintegrate rapidly in water are contained in depressions in sheets of filmic material and are enclosed by a covering sheet adhering to the filmic material." (See abstract). "The shaped articles are prepared by a process which comprises subliming solvent from a composition comprising the chemical (e.g. pharmaceutical substance) and a solution of carrier material in a solvent ..." (See column 3, Lines 21-25). "The carrier material can be any water soluble or water dispersible material that is pharmacologically acceptable or inert to the chemical and which is capable of forming a rapidly disintegratable open matrix network." (See column 2, Lines 53-57). "A particularly advantageous carrier may be formed from polypeptides such as gelatin..." (See column 2, Lines 60-62). "The solvent is preferably water but it may contain a cosolvent (such as alcohol e.g. tert-butyl alcohol) ..." (See column 3, Lines 32-34). Gregory further teaches, "A measured quantity of the composition may be added to each depression and the filmic material containing the filled material then cooled ... When the contents of the depressions are frozen the filmic and contents may be subjected to reduced pressure ...to aid the sublimation." (See column 5, Lines 12-20). "A large sheet of filmic material ... containing numerous depressions may be subjected to the freeze drying procedure and the covering sheet may then be adhered to it." (See column 5, Lines 24-26). The method of formulation of a pharmaceutically active agent into a readily dissolving, orally administered tablet taught by Gregory et al.

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has the inherent property of rendering the active substance less soluble and more palatable. Therefore, it would be expected that an identical process, such as that taught by Gregory et al., would necessarily also render the active substance less soluble and more palatable.

***Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)***

Gregory et al. lacks a teaching of the active substance being domperidone. Ince et al. cure this deficiency. Gregory et al. lacks an anticipatory teaching of freeze-drying to remove solvent following freezing of the composition. Gregory et al. however makes such a teaching obvious.

Ince et al. teaches a composition that comprises a 4-hydroxy phenethylamines and optionally other pharmaceutically active substances. (See abstract and column 10, Lines 59-64). One such example of an additional compound to be used in the composition is domperidone. (See column 11, Lines 1-11). The composition can be made into tablets and capsules further include adjuvants and carriers including gelatin. (See column 11, Lines 32-37).

***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Gregory et al. and Ince et al. One would have been motivated to do this so that the composition of Ince et al. could be formed into a blister pack of tablets for dispensing to a patient. Wherein the advantage of doing so by

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the process of Gregory et al. would “enable packages of the shaped articles to be produced in which the handling of the individual shaped articles may be eliminated until the user ... removes the product from the depression in the package immediately prior to use.” (See Gregory et al. column 4, Lines 1-6). Gregory et al. teaches the use of freeze-drying and freezing composition in the package. However, Gregory et al does not teach freeze-drying followed by the freezing step. It would have been obvious to one of ordinary skill in the art to combine the two steps. One would have been motivated to do this in order to get the additive effect of the steps in removing the solvent from the composition. For the foregoing reasons the instantly claimed process and composition are made obvious.

Response to Applicants Arguments

Applicant argues that Gregory et al. does not teach rendering an active substance less soluble either prior to or while forming a solution or suspension in the presence of a carrier material and that the teaching of Ince et al. does not cure this deficiency. Applicant’s argument has been fully considered but found not to be persuasive. Ince et al. teach the formulation of a tablet comprising domperidone as a free base. The applicants own specification indicates that addition of the free base domperidone to the other agents for tableting renders the domperidone less soluble. (See specification page 16, example 2). It is the examiners position that the method taught by Gregory et al. would necessarily result in rendering free base domperidone less soluble since it is identical to the method instantly claimed. For the foregoing

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reasons the rejection of claims 24, 26-30, 32-34, and 36 under 35 U.S.C. 103(a) is maintained.

2. The rejection of claims 24-34, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gregory et al. (US 4305502, Published 12/15/1981) in view of Mughal (US 4465838, Published 08/14/1984) **is maintained**.

Applicant Claims

Applicant claims a process for the preparation of a solid, rapidly disintegrating dosage form comprising a pharmaceutically active substance in an aqueous or alcohol solvent and further comprising a carrier materials (i.e. gelatin), rendering the active substance less soluble. The process further comprises the composition being filled into a plurality of mold pockets in a film and frozen, which is further freeze-dried, or vacuum dried to remove the solvent.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Gregory et al. teaches, "The invention relates to packages containing shaped articles carrying chemicals, particularly to pharmaceutical dosage forms carrying pharmaceuticals. The shaped articles, which disintegrate rapidly in water are contained in depressions in sheets of filmic material and are enclosed by a covering sheet adhering to the filmic material." (See abstract). "The shaped articles are prepared by a process which comprises subliming solvent from a composition comprising the chemical (e.g. pharmaceutical substance) and a solution of carrier material in a solvent ..." (See

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column 3, Lines 21-25). "The carrier material can be any water soluble or water dispersible material that is pharmacologically acceptable or inert to the chemical and which is capable of forming a rapidly disintegratable open matrix network." (See column 2, Lines 53-57). "A particularly advantageous carrier may be formed from polypeptides such as gelatin..." (See column 2, Lines 60-62). "The solvent is preferably water but it may contain a cosolvent (such as alcohol e.g. tert-butyl alcohol) ..." (See column 3, Lines 32-34). Gregory further teaches, "A measured quantity of the composition may be added to each depression and the filmic material containing the filled material then cooled ... When the contents of the depressions are frozen the filmic and contents may be subjected to reduced pressure ...to aid the sublimation." (See column 5, Lines 12-20). "A large sheet of filmic material ... containing numerous depressions may be subjected to the freeze drying procedure and the covering sheet may then be adhered to it." (See column 5, Lines 24-26). In a preferred example Gregory et al. teaches that the active agent is oxaprozin and Lorazepam. (See column 5, example 1 and column 6, example 3). The method of formulation of a pharmaceutically active agent into a readily dissolving, orally administered tablet taught by Gregory et al. has the inherent property of rendering the active substance less soluble and more palatable. Therefore, it would be expected that an identical process, such as that taught by Gregory et al., would necessarily also render the active substance less soluble and more palatable.

***Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)***

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Gregory et al. lacks a teaching of the active substance being presented in a less soluble form prior to formation of said system. Mughal cures this deficiency.

Mughal teaches that oxaprozin has a very bitter taste and teaches a method of forming a insoluble calcium oxaprozin which is less bitter. (See column 1, Line 11 and Lines 28-40).

***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art to combine the teachings of Gregory et al. with Mughal. One would have been motivated to do so because Mughal teaches the use of this insoluble oxaprozin would provide a tablet that does not have a bitter taste. For the foregoing reasons the instantly claimed process and composition are made obvious.

Response to Applicants Arguments

Applicant argues that Gregory et al. does not teach rendering an active substance less soluble either prior to or while forming a solution or suspension in the presence of a carrier material and that the teaching of Mughal et al. does not cure this deficiency since it would be counterintuitive for one to combine the teachings of Gregory et al. with Mughal et al. Applicant argues that given Gregory et al.'s preference for readily soluble active ingredients one of ordinary skill in the art would not look to decrease the solubility of the intended active agent. Applicant's argument has been fully considered but found not to be persuasive. Mughal et al. teach that oxaprozin should be

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formed into calcium oxaprozin which is less soluble in order to reduce the bitter taste prior to tableting. With regard to Applicant's assertion that it would be counterintuitive for one to render the active less soluble given Gregory et al.'s logical preference for soluble active agents, it is the Examiners position that Gregory et al. has not indicate any such preference and that Gregory et al. has examples using both soluble and insoluble active agents (lorazepam). Therefore, one of ordinary skill in the art would expect success in practicing the taught by Gregory et al. with both soluble and insoluble active agents. For the foregoing reasons the rejection of claims 24-34, and 37 under 35 U.S.C. 103(a) is maintained.

New Grounds of Rejection

3. Claims 35 and 38 under 35 U.S.C. 103(a) as being unpatentable over Gregory et al. (US 4305502, Published 12/15/1981) in view of Kurazumi et al. (US 5182112, Published 01/26/1993).

Applicant Claims

Applicant claims a process for the preparation of a solid, rapidly disintegrating dosage form comprising a pharmaceutically active substance in an aqueous or alcohol solvent and further comprising a carrier materials (i.e. gelatin), rendering the active substance less soluble. The process further comprises the composition being filled into a plurality of mold pockets in a film and frozen, which is further freeze-dried, or vacuum dried to remove the solvent.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Gregory et al. teaches, "The invention relates to packages containing shaped articles carrying chemicals, particularly to pharmaceutical dosage forms carrying

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pharmaceuticals. The shaped articles, which disintegrate rapidly in water are contained in depressions in sheets of filmic material and are enclosed by a covering sheet adhering to the filmic material.” (See abstract). “The shaped articles are prepared by a process which comprises subliming solvent from a composition comprising the chemical (e.g. pharmaceutical substance) and a solution of carrier material in a solvent ...” (See column 3, Lines 21-25). “The carrier material can be any water soluble or water dispersible material that is pharmacologically acceptable or inert to the chemical and which is capable of forming a rapidly disintegratable open matrix network.” (See column 2, Lines 53-57). “A particularly advantageous carrier may be formed from polypeptides such as gelatin...” (See column 2, Lines 60-62). “The solvent is preferably water but it may contain a cosolvent (such as alcohol e.g. tert-butyl alcohol) ...” (See column 3, Lines 32-34). Gregory further teaches, “A measured quantity of the composition may be added to each depression and the filmic material containing the filled material then cooled ... When the contents of the depressions are frozen the filmic and contents may be subjected to reduced pressure ...to aid the sublimation.” (See column 5, Lines 12-20). “A large sheet of filmic material ... containing numerous depressions may be subjected to the freeze drying procedure and the covering sheet may then be adhered to it.” (See column 5, Lines 24-26). The method of formulation of a pharmaceutically active agent into a readily dissolving, orally administered tablet taught by Gregory et al. has the inherent property of rendering the active substance less soluble and more palatable. Therefore, it would be expected that an identical process, such as that taught

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by Gregory et al., would necessarily also render the active substance less soluble and more palatable.

***Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)***

Gregory et al. lacks a teaching of the active substance is loperamide. Kurazumi et al. cure this deficiency.

Kurazumi et al. teach formulating an anti-diarrhea composition comprising loperamide hydrochloride, sucrose, and sodium bicarbonate which as added to a carrier composition. (See title and Column 6, example 6, Lines 44-63). Such a composition has the advantage of having an enhance activity and lower side effects. (See column 2, Lines 12-17).

***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Gregory et al. and Kurazumi et al. One would have been motivated to do this so that the composition of Kurazumi et al. could be formed into a blister pack of tablets for dispensing to a patient. Wherein the advantage of doing so by the process of Gregory et al. would “enable packages of the shaped articles to be produced in which the handling of the individual shaped articles may be eliminated until the user ... removes the product from the depression in the package immediately prior to use.” (See Gregory et al. column 4, Lines 1-6). With regard to the limitation that the active agent be rendered less soluble prior to or at the same time as

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the formation of the system, it is the Examiners position that this is implicit to the composition of Kurazami et al. since it includes sodium bicarbonate. The applicant's specification indicates that sodium bicarbonate renders loperamide hydrochloride less soluble. (See specification page 15, example 1). For the foregoing reasons the instantly claimed process and composition are made obvious.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ali Soroush whose telephone number is (571) 272-9925. The examiner can normally be reached on Monday through Thursday 8:30am to 5:00pm E.S.T.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

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